Application Number: 10/602,456
Balschmidt et al.
Filed: June 23, 2003
Attorney Docket No.: 6460.200-US
Via Facsimile No.: 571-273-8300

AMENDMENTS TO THE SPECIFICATION

(1) Kindly begin the claims, currently found on page 9, line 4 of the specification as originally filed, on a separate sheet following the presently numbered page 9.

(2) Kindly replace the paragraph beginning on page 2, line 28 through page 3, line 2, of the specification as originally filed with the following replacement paragraph:

Dimethyl sulfone which is also designated methylsulfonylmethane **(MSM)** ~~**or MSM**~~ may be prepared from dimethyl sulfoxide by oxidation. It can be obtained in highly purified form as crystals with a melting point at about 110 °C and has a well defined boiling point at 238 °C. It is commercially available at a low price. It is non-toxic and non-allergenic. Furthermore, it is very soluble in water. These properties make it very attractive for use in pharmaceutical compositions. Dimethyl sulfone is very stable and does not deteriorate the peptide in the pharmaceutical composition. Accordingly, very stable pharmaceutical compositions are provided.

(3) Kindly replace the paragraph found on page 3, lines 19-22, of the specification as originally filed with the following replacement paragraph:

The pharmaceutical composition comprises a peptide as active ingredient. In one embodiment, the peptide is human growth hormone, **glucagon-like peptide-1 (GLP-1)** ~~**GLP-1**~~, **glucagon-like peptide-2 (GLP-2)** ~~**GLP-2**~~, insulin, Factor VII, Factor VIII, erythropoeitin (EPO), glucagon, interleukin, such as interleukin-2 (IL-2), interferon-α or interferon-β, or an analogue thereof, or a derivative of any such peptide or analogue.

(4) Kindly replace the paragraph beginning on page 5, line 31 through page 6, line 3, of the specification as originally filed with the following replacement paragraph:

The formulations were stored in closed 1 ml **high-performance liquid chromatography (HPLC)** ~~HPLC~~ vials at 4 °C and at 25 °C, respectively. After storage for 10 weeks the formulations were analyzed by reverse phase HPLC on a 4.6 mm X 150 mm Waters SymmetryShield RP_8 (3.5 μm) column eluted at 30 °C by a buffer system A (0.2 M sodium sulphate, 0.04 M sodium phosphate, pH 7.2 in 10% (v/v) acetonitrile) with 19% B (70% (v/v) acetonitrile) for 21 min, then with 24% B for 30 min and finally with a linear gradient from 24% B to 39% B over 30 min.

(5) Kindly replace the paragraph found on page 6, lines 4-9, of the specification as originally filed with the following replacement paragraph:

The **area under the curve (AUC)** ~~AUC~~ for the side peaks in percentage of the total AUC for the insulin-related peaks was calculated as a measure of purity. Thus, a low number indicates a high degree of purity. The difference in purity between the human insulin solutions stored at 4 °C and 25 °C, respectively, is shown in the table **below** for each of the formulations.

Formulation	~~A% Purity~~ **Difference in % Purity**
I (dimethyl sulfone)	1.64
II (no isotonicity agent)	1.62
III (glycerol)	1.92